Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-20. (Cancelled).

21. (Previously presented) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a clostridial neurotoxin;

(b) incorporating the construct into a host cell;

(c) expressing the construct to produce the clostridial neurotoxin; and

(d) covalently attaching the clostridial neurotoxin to a targeting moiety which comprises substance P, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

22. (Original) The method of claim 21, wherein the covalent linkage includes one or more spacer components.

23-35. (Cancelled)

36. (Previously presented) A plasmid encoding a clostridial neurotoxin, comprising:

(a) a first nucleotide sequence region comprising;

(i) a first portion encoding an amino acid sequence region

comprising a targeting moiety that comprises substance P and is able to specifically bind to receptors on cells under physiological conditions; and (ii) a second portion encoding an amino acid sequence region comprising a translocation element able to facilitate the transfer of a polypeptide across an endosome membrane; and

(b) a second nucleotide sequence region encoding an additional amino acid sequence region comprising a therapeutic element having an intracellular protease biological activity when released into the cytoplasm of a target cell, and an origin of replication directing plasmid replication by a host cell, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

37. (Previously presented) A method of making a clostridial neurotoxin comprising:

(a) inserting the plasmid of claim 36 into a suitable host cell,

(b) growing the host cell in culture, and

(c) permitting the host cell to express the polypeptide from the plasmid.

38-66. (Cancelled)

67. (Previously presented) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a clostridial neurotoxin;

(b) incorporating the construct into a host cell;

(c) expressing the construct to produce the clostridial neurotoxin; and

(d) covalently attaching the clostridial neurotoxin to substance P, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

68. (Previously presented) The method of claim 67, further comprising covalently attaching at least one spacer component between the clostridial neurotoxin and the substance P.

69. (Previously presented) The method of claim 67, wherein the clostridial neurotoxin is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

70. (Previously presented) The method of claim 67, wherein the clostridial neurotoxin is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

71. (Previously presented) The method of claim 67, wherein the clostridial neurotoxin is botulinum toxin serotype A.

72. (Previously presented) The method of claim 67, wherein the clostridial neurotoxin comprises an H_N and an L chain.

73. (Previously presented) The method of claim 72, wherein the H_N is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

74. (Previously presented) The method of claim 72, wherein the L chain is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

75. (Previously presented) The method of claim 72, wherein the H_N is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

76. (Cancelled)

77. (Previously presented) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a botulinum toxin serotype A;

(b) incorporating the construct into a host cell;

(c) expressing the construct to produce the botulinum toxin serotype A; and

(d) covalently attaching the botulinum toxin serotype A to substance P, wherein H_C has been removed from the botulinum toxin or modified so as to reduce the ability of the botulinum toxin to bind to a receptor for the H_C at a neuromuscular junction.

78. (Previously presented) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a botulinum toxin, wherein the portion encoding an Hc of the toxin has been removed;

(b) incorporating the construct into a host cell;

(c) expressing the construct to produce the botulinum toxin; and

(d) covalently attaching the botulinum toxin to substance P.

79-80. (Cancelled)